

Section III
Remarks

A. Regarding the Amendments

Claim 6 has been amended as set forth in the above Complete Listing of the Claims. As amended, the claims are supported by the specification and the original claims. No new matter has been added, as defined by 35 U.S.C. § 132.

Upon entry of the amendments, claims 1-15 will be pending, of which claims 1-5 and 7-11 are withdrawn. Rejoinder of claims 7-9 is requested below.

B. Requirement for Restriction

The Office Action mailed January 25, 2007 requires affirmation of applicant's election of claims in the present application. By the present response, applicant affirms election of Group II, as set forth in the Amendment and Response mailed October 6, 2007. The election is made with traverse, for the reasons set forth in that Response.

Pending claim 9 was not included in the original oral restriction and is not included in the present Requirement for Restriction. Applicant assumes that claim 9 should be included with claims 7 and 8, as claim 9 depends from the method of claim 8.

Applicant respectfully requests reconsideration of the inclusion of claims 7 and 8 in Group I. Claims 1-5 of Group I are directed to isolated nucleic acid molecules encoding cysplasin and claims 7 and 8 are directed to methods of making proteins exhibiting properties of cysplasin. These claims are not properly grouped together. Claims 7 and 8 are more properly included in Group II, with claims 6, 12 and 13, directed to isolated proteins. Claims 7, 8 and 9 (not presently included in any Group of the Requirement for Restriction) are directed to methods of making the proteins of claims 6, 12 and 13. Inclusion of claims 7-9 in Group II is therefore respectfully requested.

Accordingly, rejoinder of method claims 7-9 with elected Group II claims 6, 12 and 13 is respectfully requested.

The examiner's entry of the Amendment and Response amending claims 6-8 and adding new claims 14-15 is noted.

C. Objection to the Drawings

The drawings identified as Figures 4, 7-9 and 12 have been objected to under 37 C.F.R. § 1.83(a) as failing “to show the details as described in the specification.” Attached hereto is Appendix A, containing Replacement Sheets of drawings for FIGS. 3-10 and 12.

By the attached Replacement Sheets, the objections to the drawings have been addressed. Specifically, drawings 4, 7-9 and 12 have been replaced by Replacement Sheets that clarify the figures set forth therein. On the Replacement Sheet for Figure 7, captions have been added to identify the panels of the figure, in accordance with the description in the specification as filed, at page 6, lines 21-31. Replacement Sheets for Figures 4, 8, 9 and 12 are also in accordance with the respective description in the specification, as filed.

The Figures, as submitted on the attached Replacements Sheets, are therefore in accordance with the requirements of 37 C.F.R. § 1.83(a). Withdrawal of the objection to the drawings is therefore respectfully requested.

D. Sequence Listing Requirements

The application is noted by the examiner as not being fully compliant with the requirements of 37 C.F.R. §§ 1.821-1.825, for containing sequences that are not identified by SEQ ID NO. In the Amendments section above, the specification has been amended to properly identify each sequence in the application by SEQ ID NO, present in the Sequence Listing as filed.

Specifically, amendments have been made to the descriptions of Figures 2(a), 2(b), 10, and 11 and to the paragraphs at page 21 and 25, as identified by the examiner.

As amended, the application is fully compliant with the requirements of 37 C.F.R. §§ 1.821-1.825.

E. Objections to the Specification

As set forth above in Section I, the specification has been amended to correct the informalities identified by the examiner. In particular, the title has been amended to italicize the term “*Aplysia punctata*,” the heading for the figures has been amended to read “*BRIEF DESCRIPTION OF THE DRAWINGS*,” and the description of Figure 4 has been amended to

refer to the three lanes of the gel in that Figure as the left lane, the middle lane and the right lane, as suggested by the examiner.

As the suggested corrections have been made, withdrawal of the objections to the specification is respectfully requested.

F. Objections to the Claims

Claim 6 has been objected to in the Office Action mailed January 25, 2007 as containing an informality, in that the claim required a comma to be added in part c), as identified by the examiner. Such an amendment has been made to claim 6, as set forth above in Section II.

As the suggested correction has been made, withdrawal of the objection to claim 6 is respectfully requested.

G. Rejection of Claims 6 and 12-15 Under 35 U.S.C. § 112, first paragraph

Claims 6 and 12-15 are rejected in the Office Action mailed January 25, 2007 as failing to comply with the written description and enablement provisions of 35 U.S.C. § 112, first paragraph. In particular the rejection is based on the recitation of part d) of claim 6. As set forth above in Section II, claim 6 has been amended such that it no longer contains part d). In light of this amendment, the rejection of claim 6 and claims 12-15 dependent therefrom is respectfully submitted to be moot.

H. Rejection of Claims 6 and 12-15 Under 35 U.S.C. § 102

Claims 6, 12, 13, and 15 are rejected in the Office Action mailed January 25, 2007 under 35 U.S.C. § 102(b), as anticipated by Takamatsu et al., FEBS Lett., 377:373-76 (1995), hereinafter “Takamatsu et al.,” as evidenced by Kamiya et al., Experientia, 42:1065-67 (1986), hereinafter “Kamiya et al.”

Anticipation of a claim requires the disclosure in a single prior art reference of each element of the claim under consideration. (In re Spada, 15 USPQ2d 1655 (Fed. Cir., 1990); In re Bond, 15 USPQ2d 1566 (Fed. Cir., 1990).)

As set forth in the Office Action mailed January 25, 2007, Takamatsu et al. teach a 556 amino acid protein with anti-tumor and anti-microbial activity isolated from a DNA clone, which shows

about 74% identity to amino acids 20 to 558 of SEQ ID NO: 1 of the present application. This protein of Takamatsu et al. characterized in the Office Action as a derivative of SEQ ID NO: 1, and therefore anticipatory of part d) of claim 6.

As set forth above in Section II, claim 6 has been amended such that it no longer contains part d). Takamaytsu et al. do not anticipate claim 6, as amended, as Takamatsu et al. do not describe all elements of claim 6. Specifically, Takamatsu et al. do not provide an isolated protein encoded by a nucleic acid molecule selected from the group consisting of: a nucleic acid molecule encoding a protein comprising the amino acid sequence from position 20 or 53 to position 558 of SEQ ID NO: 1, a nucleic acid molecule comprising the sequence of SEQ ID NO: 5; and a nucleic acid molecule the nucleic acid sequence of which deviates from the nucleic sequences specified in (a) or (b) due to the degeneration of the genetic code.

Claims 12, 13 and 15 depend from independent claim 6 and therefore include all elements of that independent claim. As Takamatsu et al. do not disclose all elements of claim 6, Takamatsu cannot disclose all elements of dependent claims 12, 13 or 15. Accordingly, Takamatsu et al. do not anticipate claims 6, 12, 13 and 15. Withdrawal of the rejection of claims 6, 12, 13 and 15 under 35 U.S.C. § 102 (b), as being anticipated by Takamatsu et al., is respectfully requested.

Additionally, claims 6 and 15 are rejected in the Office Action mailed January 25, 2007 under 35 U.S.C. § 102(b), as anticipated by Petzelt (NCBI Accession No. AJ304802). Applicants respectfully disagree.

The Petzelt sequence cited by the examiner is cited as being 100% identical to SEQ ID NO: 1. SEQ ID NO: 1 itself is not claimed by the currently pending claims of the invention, as amended claim 6 recites a protein with a deleted or non-functional secretory signal sequence. SEQ ID NO: 1 contains a functional secretory signal sequence and is therefore not within the scope of amended claim 6. Part a) of amended claim 6 recites a nucleic acid molecule encoding a portion of SEQ ID NO: 1, from amino acid residues 20-558 or 53-558, wherein the resulting encoded protein has a deleted or non-functional secretory signal sequence. As is well described throughout the specification, the ranges of amino acid residues 20-558 or 53-558 of SEQ ID NO: 1 were selected because either or both residues 20 or 53 may be the cleavage site for cleavage of the protein by the signal peptide (as shown from the data in Figure 10). It is essential to the invention that the resulting protein has either a non-functional secretory signal sequence or that it lacks the secretory signal sequence. Independent claim 6 has been amended to reflect this

functional characteristic of the claimed protein.

As such, amended claim 6 of the present invention recites a protein with a deleted or non-functional secretory signal sequence. Petzelt, however, does not disclose an amino acid sequence with a deleted or non-functional secretory signal sequence. Petzelt, in fact, discloses a sequence identical to SEQ ID NO: 1, which is known to contain a functional secretory signal sequence. Accordingly, the sequence disclosed by Petzelt cannot anticipate the sequences of claim 6. As dependent claim 15 depends from independent claim 6, Petzelt also cannot anticipate claim 15.

As Petzelt does not describe a protein with a deleted or non-functional secretory signal sequence as set forth in claims 6 and 15, Petzelt does not anticipate the claimed invention. Accordingly, withdrawal of the rejection of claims 6 and 15 under 35 U.S.C. § 102 (b), as being anticipated by Petzelt, is respectfully requested.

I. Rejection of Claims 12 and 13 Under 35 U.S.C. § 103

Claims 12 and 13 are rejected in the Office Action mailed January 25, 2007 under 35 U.S.C. § 103(a) as being unpatentable over Petzelt (as cited above) in view of Yamazaki, Comp. Biochem. Physiol. C, 105(2):141-6 (1993), hereinafter “Yamazaki,” and Petzelt, U.S. Patent No. 6,171,818, hereinafter “the ‘818 patent.”

It is elemental law that in order for an invention to be obvious, the difference between the subject matter of the application and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard for a proper §103 rejection, all claim limitations must be disclosed or derivable from the cited combination of references. See MPEP §2143:

“2143 Basic Requirements of a Prima Facie Case of Obviousness

“To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The combined references of Petzelt in view of Yamazaki and further in view of the ‘818 patent

do not disclose all claim elements of rejected claims 12 and 13. Accordingly, Petzelt in view of Yamazaki and further in view of the '818 patent fail to provide any derivative basis for the claimed invention. Accordingly, no basis of *prima facie* obviousness of the claimed invention is presented by such cited references.

While claim 12 recites a pharmaceutical composition, that claim depends from claim 6, such that claim 12 recites a pharmaceutical composition comprising a protein of claim 6. As set forth in detail above, Petzelt does not disclose a protein such as that set forth in claim 6 that lacks a functional secretory signal sequence. Furthermore, neither Yamazaki nor the '818 patent disclose a protein lacking a functional secretory signal sequence. Accordingly, the combined disclosures of these references do not provide a pharmaceutical composition comprising a protein of claim 6.

Furthermore, it is acknowledged that the combination of the Petzelt and Yamazaki references do not "teach cysplasin or any other proteins from *Aplysia punctata* and/or suggest to put these into a pharmaceutical composition." (Office Action mailed January 25, 2007, page, 17.) In order to support this lack of disclosure, the '818 patent is cited as "teach[ing] a protein isolated from *Aplysia punctata* which has anti-tumor activity." (Office Action mailed January 25, 2007, page, 17.) However, nowhere in the combination of Petzelt in view of Yamazaki and further in view of the '818 patent is a pharmaceutical composition disclosed nor is cysplasin isolated from *Aplysia punctata*. One of skill could not have derived the present invention from the disclosures of the cited references. From the combination of references, one of skill could not have derived use of potentially pharmacologically active proteins in a pharmaceutical composition. While the combination of references may show a single protein isolated from *Aplysia punctata* with anti-tumor activity, it does not show isolation of additional proteins from *Aplysia punctata*, assessment of additional proteins for anti-tumoral activity, nor does it show determination of pharmaceutical efficacy or potentially pharmacologically active proteins. The present invention would therefore not have been derivable from the cited combination of references without further inventive steps.

As Petzelt in view of Yamazaki and further in view of the '818 patent does not provide any logical basis for the pharmaceutical composition recited in claims 12 and 13, Petzelt in view of Yamazaki and further in view of the '818 patent does not render the claimed invention obvious. Accordingly, withdrawal of the rejection of claims 12 and 13 under 35 U.S.C. § 103(a) as obvious over Petzelt in view of Yamazaki and the '818 patent is respectfully requested.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 6 and 12-15 are patentably distinguished over the art, and are in form and condition for allowance. The Examiner is requested to favorably consider the foregoing and to responsively issue a Notice of Allowance.

The time for responding to the January 25, 2007 Office Action without extension was set at three months, or April 25, 2007. Applicants hereby request a one month extension of time under 37 C.F.R. § 1.136 to extend the deadline for response to and including May 25, 2007. Payment of the extension fee of \$60.00 specified in 37 C.F.R. § 1.17(a)(2), as applicable to small entity, is authorized by the enclosed Credit Card Payment Form PTO-2038. Should any additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the Examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

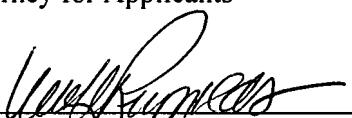
Respectfully submitted,



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Enclosures:

Appendix A [10 pgs.]
Credit Card Payment Form PTO-2038 [1 pg.]

The USPTO is hereby authorized to charge any deficiency or credit any overpayment of fees properly payable for this document to Deposit Account No. 08-3284

APPENDIX A